

**CLAIMS:**

1. A method for detecting a target oligonucleotide in a sample, comprising:
  - (a) providing a sensor device having a sensing interface carrying capturing oligonucleotides having each a nucleotide sequence complementary in at least a stably hybridizing portion thereof to a first portion of the target oligonucleotides wherein said sensor device comprises an electrochemical probe carrying the sensing interface;
  - (b) providing verification oligonucleotides having each a nucleotide sequence complementary in at least a stably hybridizing portion thereof to a second portion of the target oligonucleotide, other than said first portion;
  - (c) contacting the sample with the sensing interface under conditions such as to allow the target oligonucleotides, if present in the sample, to hybridize to the capturing oligonucleotides;
  - (d) prior to (c) or thereafter, allowing the verification oligonucleotides to hybridize to the target oligonucleotides if present in the sample; and
  - (e) detecting the presence of said verification oligonucleotides on the sensing interface.
2. The method of Claim 1, wherein said detection is based on Faradaic impedance spectroscopy or amperometric measurements.
3. The method of either of Claims 1 or 2, wherein the sequence complementary to at least a stably hybridizing portion of the target oligonucleotide is of about 12 nucleotides.
4. The method according of any one of Claims 1-3, wherein the verification oligonucleotide is conjugated to a recognition agent which can specifically bind to a signal-amplifying agent, and step (e) of the method comprises:
  - (e1) contacting the sensing interface with said signal-amplifying agent;
  - (e2) detecting the presence of said signal-amplifying agent on the sensing interface.
5. The method of Claim 4, wherein said recognition agent is biotin and said signal amplifying agent comprises avidin.
6. The method of any one of Claims 1-3, wherein said verification oligonucleotide is bound to or complexed with a signal-amplifying agent, and step

(e) comprises detecting of presence of the signal-amplifying agent on the sensing interface.

7. The method of any one of Claims 1-3, wherein the verification oligonucleotide comprises a first recognition agent which specifically binds to a recognition partner to form a recognition couple, step (e) of the method comprises the following steps:

- (e1) contacting said sensing interface with said recognition partner;
- (e2) contacting said sensing interface with a signal-amplifying agent comprising a second recognition agent, which may be the same or different as the first recognition agent, which can also bind to said recognition partner; and
- (e3) detecting presence of said signal-amplifying agent on said sensing interface.

8. The method of Claim 7, comprising the following step between steps (e2) and (e3):

- (e2.1) repeating steps (e1) and (e2) one or more times.

9. The method of any one of Claims 4-8, wherein said signal-amplifying agent comprises an enzyme which catalyzes a reaction yielding an insoluble reaction product, and step (e) comprises:

- (ea) providing conditions permitting catalytic activity of said enzyme to yield formation of said insoluble reaction product; and
- (eb) detecting the presence of said insoluble reaction product on said sensing interface.

10. The method of any one of Claims 4-8, wherein said signal-amplifying agent comprises a moiety or a particle which directly increases the mass immobilized on the sensing surface, the method comprises in step (e):

- (ea) detecting the presence of said moiety or particle on said sensing interface.

11. The method of Claim 10, wherein said moiety is a molecule or a super molecular structure.

12. A system for detecting a target oligonucleotide in a sample, comprising:

(i) a sensor device having a sensing interface carrying capturing oligonucleotides having each a nucleotide sequence complementary in at least a stably hybridizing portion thereof to a first portion of the target oligonucleotides wherein said sensor device is an electrochemical electrode carrying said sensing interface;

(ii) verification oligonucleotides having each a nucleotide sequence complementary in at least a stably hybridizing portion thereof to a second portion of the target oligonucleotide, other than said first portion; and

(iii) a detecting means comprising one or both of apparatus and reagents for detecting a verification oligonucleotide bound to the sensing interface.

13. The system of Claim 12, wherein when the system comprises an apparatus, said apparatus is adapted for the performance of an electrochemical measurement.

14. The system of either of Claims 12 or 13, wherein said capturing oligonucleotide has a nucleotide sequence complementary to said first portion which has a length of about 12 nucleotides.

15. The system of any one of Claims 12-14, wherein the verification oligonucleotide is conjugated to a recognition agent which specifically binds to a signal-amplifying agent.

16. The system of Claim 15, wherein said recognition agent is biotin and said signal-amplifying agent comprises avidin.

17. The system of any one of Claims 12-14, wherein the verification oligonucleotide is conjugated or complexed with a signal-amplifying agent.

18. A system of any one of Claims 12-14, wherein the verification oligonucleotide is conjugated to a first recognition agent, which specifically binds to a recognition partner, the recognition partner being capable of binding also to a second recognition agent, being the same or different from said first recognition agent; the system further comprises a signal amplifying agent comprising a second recognition agent.

19. A system of Claim 18, when said first and said second recognition agents are biotin and where said recognition partner is avidin or streptavidin.

20. A system of any one of Claims 12-19, wherein said signal-amplifying agent comprises an enzyme which catalyzes a reaction yielding an insoluble reaction product.

21. A system of any one of Claims 12-19, wherein said signal-amplifying agent comprises a particle or moiety which directly increases the mass immobilized on the sensing interface.
22. For use in the method of any one of Claims 1-11 or the system of any one of Claims 12-21, a reagent being at least one member of the group consisting of:
- (i) said verification oligonucleotide;
  - (ii) an amplifying agent for amplifying the signal resulting from binding of said verification oligonucleotide to said sensing interface.
23. A method for detecting a target oligonucleotide in a sample, comprising:
- (a) providing a sensor device having a sensing interface carrying capturing oligonucleotides having each a nucleotide sequence complementary in at least a stably hybridizing portion thereof to a first portion of the target oligonucleotides;
  - (b) providing verification oligonucleotides having each a nucleotide sequence complementary in at least a stably hybridizing portion thereof to a second portion of the target oligonucleotide, other than said first portion, wherein the verification oligonucleotide is capable of binding to a signal-amplifying agent comprising a liposome,
  - (c) contacting the sample with the sensing interface under conditions so as to allow the target oligonucleotides, if present in the sample, to hybridize to the capturing oligonucleotides;
  - (d) prior to (c) or thereafter, allowing the verification oligonucleotides to hybridize to the target oligonucleotides if present in the sample;
  - (e) contacting the sensing interface with said signal-amplifying agent; and
  - (f) detecting the presence of said signal-amplifying agent on the sensing interface.
24. The method of Claim 23, wherein said sensor device comprises an electrochemical probe carrying the sensing interface.
25. The method of Claim 24, wherein said detection is based on Faradaic impedance spectroscopy or amperometric measurements.
26. The method of Claim 23, wherein said sensor device comprises a microbalance quartz-crystal probe carrying the sensing interface.

27. The method of Claim 26, wherein said detection is based on a microgravimetric quartz-crystal microbalance (QCM) analysis.
28. The method of any one of Claims 23-27, wherein the sequence complementary to at least a stably hybridizing portion of the target oligonucleotide is of about 12 nucleotides.
29. The method according of any one of Claims 23-28, wherein the verification oligonucleotide is conjugated to a recognition agent which can specifically bind to said signal-amplifying agent.
30. The method of Claim 29, wherein said recognition agent is biotin and said signal amplifying agent comprises avidin.
31. The method of any one of Claims 23-28, wherein said verification oligonucleotide is bound to or complexed with said signal-amplifying agent.
32. The method of any one of Claims 23-28, wherein the verification oligonucleotide comprises a first recognition agent which specifically binds to a recognition partner to form a recognition couple, step (e) of the method comprising the following steps:
- (e1) contacting said sensing interface with said recognition partner;
  - (e2) contacting said sensing interface with said signal-amplifying agent comprising a second recognition agent, which may be the same or different as the first recognition agent, which can also bind to said recognition partner.
33. The method of Claim 32, comprising the following step after step (e2):
- (e2.1) repeating steps (e1) and (e2) one or more times.
34. A system for detecting a target oligonucleotide in a sample, comprising:
- (i) a sensor device having a sensing interface carrying capturing oligonucleotides having each a nucleotide sequence complementary in at least a stably hybridizing portion thereof to a first portion of the target oligonucleotides;
  - (ii) verification oligonucleotides having each a nucleotide sequence complementary in at least a stably hybridizing portion thereof to a second portion of the target oligonucleotide, other than said first portion, wherein the verification oligonucleotide is capable of binding to a signal-amplifying agent comprising a liposome; and

(iii) a detecting means comprising one or both of apparatus and reagents for detecting a verification oligonucleotide bound to the sensing interface, wherein said detecting means comprises said signal-amplifying agent comprising a liposome.

35. The system of Claim 34, wherein said sensor device is an electrochemical electrode carrying said sensing surface.

36. The system of Claim 34 or 35, wherein said apparatus is adapted for the performance of an electrochemical measurement.

37. The system of Claim 34, wherein said sensor device comprises a microbalance quartz-crystal probe carrying the sensing interface.

38. The system according to Claim 37, wherein said detection is based on a microgravimetric quartz-crystal microbalance (QCM) analysis.

39. The system of Claims 34-38, wherein said capturing oligonucleotide has a nucleotide sequence complementary to said first portion which has a length of about 12 nucleotides.

40. The system of any one of Claims 34-39, wherein the verification oligonucleotide is conjugated to a recognition agent which specifically binds to the signal-amplifying agent.

41. The system of Claim 40, wherein said recognition agent is biotin and said signal-amplifying agent comprises avidin.

42. The system of any one of Claims 34-39, wherein the verification oligonucleotide is conjugated or complexed with the signal-amplifying agent.

43. A system of any one of Claims 34-39, wherein the verification oligonucleotide is conjugated to a first recognition agent, which specifically binds to a recognition partner, the recognition partner being capable of binding also to a second recognition agent, being the same or different from said first recognition agent; the system further comprises the signal amplifying agent comprising a second recognition agent.

44. A system of Claim 43, when said first and said second recognition agents are biotin and where said recognition partner is avidin or streptavidin.

45. For use in the method of any one of Claims 23-33 or the system of any one of Claims 34-44, a reagent being at least one member of the group consisting of:

- (i) said verification oligonucleotide;

項目	単位	1990年	1991年	1992年	1993年	1994年	1995年	1996年	1997年	1998年	1999年	2000年	2001年	2002年	2003年	2004年	2005年	2006年	2007年	2008年	2009年	2010年	2011年	2012年	2013年	2014年	2015年	2016年	2017年	2018年	2019年	2020年	2021年	2022年	2023年	2024年	2025年	2026年	2027年	2028年	2029年	2030年	2031年	2032年	2033年	2034年	2035年	2036年	2037年	2038年	2039年	2040年	2041年	2042年	2043年	2044年	2045年	2046年	2047年	2048年	2049年	2050年	2051年	2052年	2053年	2054年	2055年	2056年	2057年	2058年	2059年	2060年	2061年	2062年	2063年	2064年	2065年	2066年	2067年	2068年	2069年	2070年	2071年	2072年	2073年	2074年	2075年	2076年	2077年	2078年	2079年	2080年	2081年	2082年	2083年	2084年	2085年	2086年	2087年	2088年	2089年	2090年	2091年	2092年	2093年	2094年	2095年	2096年	2097年	2098年	2099年	2100年																																																																		
総人口	人	12,100,000	12,200,000	12,300,000	12,400,000	12,500,000	12,600,000	12,700,000	12,800,000	12,900,000	13,000,000	13,100,000	13,200,000	13,300,000	13,400,000	13,500,000	13,600,000	13,700,000	13,800,000	13,900,000	14,000,000	14,100,000	14,200,000	14,300,000	14,400,000	14,500,000	14,600,000	14,700,000	14,800,000	14,900,000	15,000,000	15,100,000	15,200,000	15,300,000	15,400,000	15,500,000	15,600,000	15,700,000	15,800,000	15,900,000	16,000,000	16,100,000	16,200,000	16,300,000	16,400,000	16,500,000	16,600,000	16,700,000	16,800,000	16,900,000	17,000,000	17,100,000	17,200,000	17,300,000	17,400,000	17,500,000	17,600,000	17,700,000	17,800,000	17,900,000	18,000,000	18,100,000	18,200,000	18,300,000	18,400,000	18,500,000	18,600,000	18,700,000	18,800,000	18,900,000	19,000,000	19,100,000	19,200,000	19,300,000	19,400,000	19,500,000	19,600,000	19,700,000	19,800,000	19,900,000	20,000,000	20,100,000	20,200,000	20,300,000	20,400,000	20,500,000	20,600,000	20,700,000	20,800,000	20,900,000	21,000,000	21,100,000	21,200,000	21,300,000	21,400,000	21,500,000	21,600,000	21,700,000	21,800,000	21,900,000	22,000,000	22,100,000	22,200,000	22,300,000	22,400,000	22,500,000	22,600,000	22,700,000	22,800,000	22,900,000	23,000,000	23,100,000	23,200,000	23,300,000	23,400,000	23,500,000	23,600,000	23,700,000	23,800,000	23,900,000	24,000,000	24,100,000	24,200,000	24,300,000	24,400,000	24,500,000	24,600,000	24,700,000	24,800,000	24,900,000	25,000,000	25,100,000	25,200,000	25,300,000	25,400,000	25,500,000	25,600,000	25,700,000	25,800,000	25,900,000	26,000,000	26,100,000	26,200,000	26,300,000	26,400,000	26,500,000	26,600,000	26,700,000	26,800,000	26,900,000	27,000,000	27,100,000	27,200,000	27,300,000	27,400,000	27,500,000	27,600,000	27,700,000	27,800,000	27,900,000	28,000,000	28,100,000	28,200,000	28,300,000	28,400,000	28,500,000	28,600,000	28,700,000	28,800,000	28,900,000	29,000,000	29,100,000	29,200,000	29,300,000	29,400,000	29,500,000	29,600,000	29